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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,841	08/31/2005	Alexander Gaiger	CRX494-3	9134

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GLOBAL PATENTS -US, UW2220
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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
02/16/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/501,841	GAIGER ET AL.	
	Examiner	Art Unit	
	KAREN CANELLA	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *17,21-28,32,33 and 54* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *17, 21-28, 32, 33 and 54* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The claims filed December 13, 2011 fail to conform to the requirements of 37 CFR 1.121. Claim 54 carries the label "New", but in fact said claim should be labeled as "Previously Presented". Appropriate correction is required in response to this Office action.

Claim 28 has been amended. Claims 17, 21-28, 32, 33 and 54 are pending and under consideration.

It is re-stated that the instant claims have an effective filing date of January 22, 2003 for the reasons set forth in the prior Office action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 17, 21-28, 32, 33 and 54 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record..

Claim 17 is vague and indefinite in the recitation of "polypeptides unrelated to SEQ ID NO: 4". It is unclear what meets and bounds determine a polypeptide related to SEQ ID NO: 4, therefore it is unclear what meets and bounds determine a polypeptide unrelated to SEQ ID NO: 4. It is unclear if "related" or "unrelated" is being assessed at the sequence level, or structural level or at the level of a particular biological function, and it is unclear what degree of variance in any of primary sequence, overall structure or specific biological function is necessary for a polypeptide to be considered related to SEQ ID NO:4 therefore it is unclear what degree of variance in any of primary sequence, overall structure or specific biological function is necessary for a polypeptide to be considered unrelated to SEQ ID NO:4.

Applicant argues that the word unrelated is used in conjunction with detectable and "specifically binds" and that the application defines the term "binding" when the binding

constant for complex formation exceeds about 10^3L/mol. Applicant concludes that a polypeptide unrelated to SEQ ID NO: 4 is a peptide having a binding constant of less than 10^3L/mol. This has been considered but not found persuasive. The fact that the antibody is considered to specifically bind or not at a binding constant of 10^3L/mol does not contribute to establishing the metes and bounds of what constitutes a peptide unrelated to SEQ ID NO: 4.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 17, 21-23, 32, 33 and 54 under 35 U.S.C. 102(b) as being anticipated by Schneider et al (WO 01/24811, reference of the IDS filed 6/11/2007) is maintained for reasons of record.

Claim 17 is drawn to a method for treating chronic lymphocytic leukemia in a mammalian subject comprising administering to said subject an effective amount of an isolated monoclonal antibody that specifically binds to a polypeptide comprising SEQ ID NO:4, wherein said antibody does not detectably bind to a polypeptide unrelated to SEQ ID NO:4.

Claim 21 embodies the method of claim 17 wherein said antibody is a humanized antibody. Claim 22 embodies the method of claim 17 wherein said antibody is a chimeric antibody. Claim 23 embodies the method of claim 17, wherein said antibody is a Fab fragment. Claim 32 embodies the method of claim 17 wherein the mammalian subject is a human. Claim 33 embodies the method of claim 17 wherein the administration is intravenous.

Schneider et al disclose a method for treating a mammalian subject with a cancerous disorder, wherein said cancers express APRIL receptor or APRIL comprising the administration of anti-APRIL Receptor antibodies (page 4, lines 17-21 and page 16, lines 24-32). Schneider et al disclose examples of such cancers as including CLL (page 16, lines 33-34 and page 18, line 12). Schneider et al disclose the April receptor as SEQ ID NO: 8 (page 11, lines 3-5) which is identical to the instant SEQ ID NO: 4. Schneider et al disclose that the treatment of mammals

includes the treatment of humans (page 11, lines 6-8). Schneider et al disclose antibodies including Fab', F(ab')2, chimeric, or humanized which meets the limitations of claims 21-23. Schneider et al disclose that the anti-APRIL-Receptors antibody does not cross-react with a protein that has less than 80% homology with SEQ ID NO:8. Schneider et al disclose intravenous administration (page 4, lines 25-26). Schneider et al does not specify that the anti-April receptor antibody is a bi-specific antibody, therefore the limitations of claim 54 are met.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 17, 21-23, 26, 27, 33 and 54 under 35 U.S.C. 103(a) as being unpatentable over Schneider et al (WO 01/24811) in view of Hanna et al (U.S. 2002/0028178) is maintained for reasons of record.

Claim 26 embodies the method of claim 17 wherein said antibody further comprises a therapeutic moiety. Claim 27 embodies the method of claim 26 wherein the therapeutic moiety is a radionuclide.

Schneider et al teach as stated above. Schneider et al do not specifically teach the conjugation of a therapeutic moiety or a therapeutic moiety which is a radionuclide to the anti-APRIL-Receptor antibody

Hanna et al teach antibodies for treating B cell malignancies, including chronic lymphocytic leukemia, wherein said antibodies are conjugated to therapeutic radionuclides (paragraphs, [0025] and [0033]).

It would have been prima facie obvious at the time that the claimed invention was made to attach a therapeutic radionuclide to the anti-APRIL-Receptor antibody of Schneider et al for the treatment of CLL. One of skill in the art would have been motivated to do so by the teachings of Hanna et al regarding the attachment of therapeutic radionuclides to an antibody administered for the treatment of B cell malignancies including CLL.

The rejection of claims 17, 21-23, 26-28,33 and 54 under 35 U.S.C. 103(a) as being unpatentable over Schneider et al and of Hanna et al as applied to claims 17, 21-23, 26, 27,33 and 54 above, and further in view of Hansen et al (U.S. 6,962,702) is maintained for reasons of record.

Claim 28 embodies the method of claim 27 wherein the radionuclide is selected from the group consisting of ^{90}Y, ^{123}I, ^{125}I, ^{131}I, ^{186}Re, ^{211}At and ^{212}Bi.

The combination of Schneider et al and Hanna et al render obvious the instant claims to the extent that anti-April-R antibodies are conjugated to a therapeutic radionuclide. The combination does not specifically teach the radionuclides of ^{90}Y, ^{123}I, ^{125}I, ^{131}I, ^{186}Re, ^{211}At or ^{212}Bi.

Hansen et al teach the targeting of therapeutic radionuclides by means of conjugation to antibodies, and that particularly useful therapeutic radionuclides include ^{90}Y, ^{125}I, ^{131}I, ^{186}Re, ^{211}At and ^{212}Bi (column 17, lines 12-16).

It would have been prima facie obvious at the time that the claimed invention was made to use the therapeutic radionuclides of include ^{90}Y, ^{125}I, ^{131}I, ^{186}Re, ^{211}At and ^{212}Bi in the method of treatment rendered obvious by the combination of Schneider et al and Hanna et al. One of skill in the art would have been motivated to do so by the teachings of Hansen et al regarding the preferred radionuclides for therapeutic delivery via antibody conjugates.

The rejection of claims 17, 21-25, 33 and 54 under 35 U.S.C. 103(a) as being unpatentable over Schneider et al (WO 01/24811) in view of Shadidi et al (BBRC, 2001, Vol. 280, pp. 548-552) is maintained for reasons of record.

Claim 24 embodies the method of claim 17 wherein said antibody is an Fv fragment. Claim 25 embodies the method of claim 17 wherein said antibody is a scFv.

Schneider et al teach the invention, wherein the antibody was an antibody fragment such as a Fab' or F(ab')2 fragment. Schneider et al do not specifically teach Fv antibody fragments or scFv antibodies in the context of the invention.

Shadidi et al teach the selection of anti-leukemic scFv antibody selected from a human phage antibody library (abstract). Shadidi et al teach that human antibodies selected from phage libraries may well have a high therapeutic value relative to mouse or humanized antibodies and that human scFv antibodies can be used as delivery vectors for drugs and toxins to tumor cells (pages 550-551, bridging paragraph).

It would have been prima facie obvious at the time that the claimed invention was made to prepare scFv antibodies from human single chain phage antibody libraries. One of skill in the art would have been motivated to do so by the teachings of Shadidi et al regarding the potential high therapeutic value of the scFv antibodies as relative to mouse or humanized antibodies.

Applicant argues against the disclosure of Schneider et al stating that Schneider et al only disclose a method of treating a mammalian subject with a cancerous disorder rather than the treatment of CLL. Applicant points out that Schneider et al disclose a method of treating subjects at risk of developing cancer on page 4, lines 17-21 in contrast to the instant claims drawn to the treatment of CLL. Applicant argues that the citation of CLL as expressing APRIL on page 18, line 12 is not enabling for the method of treating CLL because Schneider et al do not disclose the level of APRIL expression. Applicant further points out that Schneider et al provide no guidelines for making an antagonistic antibody over an agonistic antibody. This has been considered but not found persuasive. Schneider et al disclose antagonists of the APRIL pathway, wherein said antagonists include anti-APRIL receptor or anti-BCMA antibodies for the treatment of cancers which express the APRIL and/or APRIL receptor (page 4, lines 1-7, page 4, line 32 to

page 5, line 2, page 16, lines 22-32). Schneider et al disclose that CLL expresses APRIL (page 18, line 12) and the use of anti-APRIL receptor antagonists for the treatment of B cell lympho-proliferative disorders (page 22, lines 8-11) and leukemias (page 35, line 7-8) which overcomes applicants argument about the level of APRIL protein expression in chronic lymphocytic leukemia. Schneider et al disclose methods of making antagonistic antibodies (page 28, lines 19-20).

All claims are rejected.

All other rejections and objections as set forth in the prior Office action are withdrawn.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAREN CANELLA whose telephone number is (571)272-0828. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on (571)272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KAREN CANELLA/
Primary Examiner, Art Unit 1643